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PATENT APPLICATION

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE HONORABLE BOARD OF PATENT APPEALS AND INTERFERENCES

In re the Application of

Philippe CROS et al.

Application No.: 08/945,731

Filed: November 10, 1997

For: NUCLEIC ACID ISOLATION



Group Art Unit: 1636

Examiner: W. Sandals

Docket No.: WPB 40330

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REPLY BRIEF

Director of the U.S. Patent and Trademark Office
Washington, D.C. 20231

Sir:

The following remarks are directed to the new points of argument raised in the Examiner's Answer mailed July 11, 2000.

In the Examiner's Answer, the Examiner states that:

The teachings of Itoh are clear that molecules can be bound at low temperatures and released at high temperatures, and in combination with the teachings of Hoffman (see especially Hoffman at column 4, line 45 bridging to column 5, line 28) one of skill in the art would immediately know that one can use the gels for binding nucleic acids at low temperatures and releasing nucleic acids at high temperatures.

Thus, in rejecting the claims, the Examiner is focusing in on the teaching of Itoh in which the materials are: (1) held in gel-like polymers at low temperatures when the gel-like polymers are swollen and (2) released from the gel-like polymers at high temperatures when the gel-like polymers are shrunk. Page 47, lines 19-24. However, as discussed in the Appeal

Brief at part VI.B.1.a., on pages 5-8, Itoh teaches at least two distinct methods for holding and releasing the various compounds to and from the polymer. In one technique, the compounds are held to the homopolymers or copolymers by intermolecular forces such as hydrogen bonds, hydrophobic bonds or the like. Page 44, lines 18-25. For this technique, Itoh teaches that the compounds are held at high temperatures and released at low temperatures, which is opposite from the process of the present invention. Page 45, lines 11-13. Since this technique is totally separate from the single technique taught in Itoh in which the compounds are held at low temperatures and released at high temperatures, it would be improper to combine the features of this technique with features of the other technique in order to achieve the present invention.

In particular, Itoh does not teach or suggest utilizing the technique in which the compounds are held at low temperatures and released at high temperatures to hold and release nucleic acids. Instead, Itoh only makes reference to holding and releasing nucleic acids in the context of holding compounds based on intramolecular forces such as hydrogen bonds, hydrophobic bonds or the like. Page 44, line 22, to page 45, line 5. As discussed above, when compounds are held by intermolecular forces, the compounds are held at high temperatures and released at low temperatures. Thus, Itoh does not teach or suggest a process in which nucleic acids are contacted with the homopolymer or copolymer at a temperature less than the LCST of the polymer.

The only teaching of holding nucleic acids at low temperatures and releasing nucleic acids at high temperatures is in Hoffman. Unlike Itoh, Hoffman does not teach or suggest holding nucleic acids to the polymer merely by absorption. Instead, to bind a nucleic acid of interest to the polymer, Hoffman teaches physically or chemically binding a complementary nucleic acid to the polymer and using that complementary nucleic acid to bind the nucleic

acid of interest to the polymer through its hybridization to the complementary nucleic acid.

Column 4, line 57 - column 5, line 19. Thus, in looking to other references to overcome the deficiencies of Hoffman, there must be motivation to utilize the feature of the other references in the unique process taught by Hoffman.

As discussed in the Appeal Brief at part VI.B.2., at pages 10-11, Hoffman does not teach or suggest many of the features on the present invention. In particular, Hoffman does not teach or suggest a copolymer of an acrylamide or acrylamide derivative monomer with a cationic functional monomer and/or a cross-linking agent. In addition, Hoffman provides no teaching or suggestion of using a pH at most equal to 7 and/or an ionic strength at most equal to 10^{-2} M during the contacting step. Thus, the Patent Office relies on Itoh and the other cited references to overcome these deficiencies of Hoffman.

In particular, the Patent Office relies on Itoh for the teaching of a copolymer of an acrylamide or acrylamide derivative monomer with a cationic functional monomer, which is cross-linked. Although the broad teachings of Itoh include a teaching of ionic monomers and cross-linkable monomers, Itoh provides no motivation to select a polymer containing cationic monomers and a cross-linking agent from the large group of homopolymers and copolymers taught therein. In the Examiner's Answer, the Examiner points to the teaching of Itoh at page 50, lines 4-11, which states that:

more selective holding and release become feasible by the use of a copolymer with an ionic monomer as the copolymer, because the use of such an ionic monomer permits introduction of either one of the ionic properties, namely, either cationic properties or anionic properties into the resultant copolymer and the ionic interaction can also be used upon holding various substances.

However, Itoh does not teach or suggest the selection of cationic rather than anionic monomers to hold nucleic acids. In particular, it is not clear how these non-specific ionic

interactions would affect the ability of nucleic acids to specifically bind to the polymers via a complementary nucleic acid, as taught by Hoffman. The cited references clearly do not teach any advantage to selecting a cationic monomer in the context of the technique described in Hoffman.

In addition, ionic interactions are a form of intermolecular interaction. Itoh clearly teaches that when the compounds are held by intermolecular forces, the compounds are held at high temperatures and released at low temperatures, which teaches away from bringing the nucleic acids into contact with the polymer at temperatures less than the LCST of the polymer.

Furthermore, in the context of the technique in which compounds are held at low temperatures and released at high temperatures, Itoh does not teach or suggest utilizing a pH of at most equal to 7 and/or an ionic strength of at most equal to 10^{-2}M during the contacting step. In the Examiner's Answer, in support of the position that Itoh teaches a pH at most equal to 7, reference is made to the teaching of Itoh of using pH to hold ampholytic electrolytes, such as amino acids or proteins. In particular, the Examiner's Answer states that:

While this section does not discuss nucleic acids, one of skill in the art would recognize the well known use of pH, with respect to the isoelectric point of a molecule to bind and release a charged molecule such as a nucleic acid, similar to the teachings of Itoh as they were applied to an amino acid or protein (emphasis added).

However, as admitted by the Examiner, Itoh does not teach or suggest how pH would affect the ability of nucleic acids to bind to the polymers, particularly Itoh does not teach or suggest how pH would affect the ability of nucleic acids to specifically bind to the polymers via a complementary nucleic acid, as taught by Hoffman. Itoh provides no motivation to select a pH at most equal to 7 to hold nucleic acids to the polymer. However, as demonstrated in

Fig. 2 of the present application, pH has a significant effect on the ability of the claimed polymers to hold the nucleic acids.

Furthermore, none of the cited references teach or suggest utilizing an ionic strength at most equal to 10^{-2}M to hold nucleic acids to the polymer. However, as demonstrated in Fig. 4 of the present application, ionic strength has a significant effect on the ability of the claimed polymer to hold nucleic acids.

In summary, the cited references, alone or as combined, do not teach all of the features of Group I. In particular, the cited references do not teach or suggest utilizing a copolymer of an acrylamide or acrylamide derivative with (1) a cationic monomer and (2) a cross-linking agent to absorb (3) nucleic acids at (4) a temperature less than the LCST of the polymer, (5) a pH at most equal to 7, and (6) an ionic strength at most equal to 10^{-2}M .

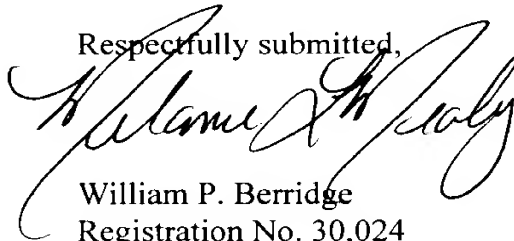
Instead, the Examiner's determination that the subject matter of Group I would have been obvious is based on hindsight reconstruction. The cited references do not teach or suggest the combination of all of the six claimed features noted above. Therefore, the rejection of the claims of Group I is improper and should be reversed. In addition, since all of the pending claims include all of the features of claim 3 of Group I, all of the pending claims are patentable for the reasons discussed above, as well as for the reasons each of Groups II-VIII were separately argued in the Appeal Brief.

In particular, with regard to Group III, the Examiner's Answer states that "[i]t should be noted that Paper No. 12 [the Appeal Brief] misstates the teachings of Hoffman at page 14, lines 13-14 [of the Appeal Brief] by stating '[a]s a result the particulate support does not consist of the functionalized, particulate polymer of claim 5'" (emphasis added). Applicants respectfully submit that this statement is not a misstatement of the teachings of Hoffman. In particular, to bind nucleic acid, Hoffman teaches physically or chemically binding a

complementary nucleic acid to the polymer. Col. 4, line 57, to col. 5, line 19. That is, the complementary nucleic acid is physically or chemically bound to the polymer and the polymer together with the bound complementary nucleic acid form a "particulate support," which is then used to bind the nucleic acid of interest. Although the complementary nucleic acid that is the first binding pair is bound to the functionalized polymer, there is no teaching as to how this is done. In particular, there is no teaching or suggestion that the first binding pair is brought into contact with the polymer at a temperature below the LCST of the polymer to absorb the first binding pair to the polymer. Instead, this technique is only used to bind the second binding pair to the polymer. By that time, the first binding pair is already bound to the polymer. Thus, in comparing the method of Hoffman to the present claims, the "particulate support" of Hoffman is the polymer with the first binding pair already bound thereto. Thus, the "particulate support" does not consist of the polymer of claim 5. Therefore, for this additional reason, the rejection of the claims of Group III is improper and should be reversed.

It is respectfully submitted that the remaining points of argument set forth in the Examiner's Answer were fully addressed in the Appellants' Appeal Brief. Therefore, for the reasons set forth herein and in the Appeal Brief, it is respectfully requested that the rejection of claims 1-3 and 5-23 under 35 U.S.C. §103 be reversed.

Respectfully submitted,



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